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# The MRC dyspnoea scale by telephone interview to monitor health status in elderly COPD patients

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**Summary**
Dyspnoea is the most common symptom associated with poor quality of life in patients affected by Chronic Obstructive Pulmonary Disease (COPD). While COPD severity is commonly staged by lung function, the Medical Research Council (MRC) dyspnoea scale has been proposed as a more clinically meaningful method of quantifying disease severity in COPD. We wished to assess whether this scale might also be useful during telephone surveys as a simple surrogate marker of perceived health status in elderly patients with COPD.

We conducted a comprehensive health status assessment by telephone survey of 200 elderly patients who had a physician diagnosis of COPD. The telephone survey contained 71 items and explored such domains as educational level, financial status, living arrangements and social contacts, co-morbid illness, and the severity and the impact of COPD on health status. Patients were categorized according to the reported MRC score: mild dyspnoea (MRC scale of 1), moderate dyspnoea (MRC scale of 2 and 3), or severe dyspnoea (MRC of 4 and 5). Deterioration in most of the recorded indicators of health status correlated with an increasingly severe MRC score. This was most evident for instrumental activities of daily living (IADL), perceived health and emotional status, pain-related limitations, limitations in social life, hospital admissions in preceding year and prevalence of most co-morbidities.

The MRC dyspnoea scale is a reliable index of disease severity and health status in elderly COPD patients which should prove useful for remote monitoring of COPD and for rating health status for epidemiological purposes.


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## Introduction

COPD is a major cause of impaired health status, disability and mortality,[1] and most current clinical practice guidelines define the severity of COPD in terms of the level of forced expiratory volume in 1 s ($FEV_1$).[2,3] However, because $FEV_1$ correlates only weakly with patient-centred outcomes such as exercise capacity, activities of daily living (ADL) and quality of life in COPD,[4–6] it is generally accepted that additional tools are required to adequately assess the impact that this disease has on patients[7,8] and the measurement of health status (also referred to as health-related quality of life) has become a commonly measured outcome in COPD clinical trials,[9] While generic questionnaires assessing health status, such as the SF-36, may have some use in COPD,[10] most recent clinical trials have used COPD-specific tools such as the St. George's Respiratory Questionnaire (SGRQ), or the Chronic Respiratory Questionnare (CRQ).[11,12] Although these health status questionnaires provide well-validated measurements of disability and handicap due to COPD, they are lengthy and have a degree of complexity that makes them too time-consuming for routine clinical use. A short form CRQ has recently been validated,[13] but like the original CRQ, it is personalized to the individual patient and so not particularly suitable for comparison amongst patients. Thus there is a need for a simpler, standardised method for scoring disability in COPD.

Dyspnoea is the most disabling symptom of COPD and the degree of dyspnoea is an important factor in the patient's perception of the illness. The Medical Research Council (MRC) scale[14] is a five-point rating scale based on the patient's perception of dyspnoea while walking distances on the level or climbing. This dyspnoea scale is simple to administer and significantly correlates with other dyspnoea scales[15] and with scores of health status.[16] It is also more responsive than $FEV_1$ in tracking changes in health status in COPD.[17] In a recent primary care survey the MRC scale was shown to have the best correlation with a new, validated COPD severity score (COPDSS),[18] and it has been used to stratify patients in pulmonary rehabilitation programs.[19] During the last decade, the MRC scale has also been used to predict mortality[20,21] and to assess the efficacy of treatment in patients affected by COPD.[22–25] It has been proposed as a fast and clinically meaningful method of categorising patients with regard to COPD-related disability,[26] and has been recommended as the preferred marker of COPD severity over $FEV_1$ in the Canadian Thoracic Society COPD clinical practice guidelines.[27]

Among numerous technological advances in medical care, the use of the telephone for health care management has increased in scope and application. Indeed, telephone surveys may be appropriate for many chronic disorders[28–32] and may provide useful information on the clinical consequences of COPD.[33] The COPDSS was originally developed from data obtained during a telephone survey of patients with established COPD.[34] Nevertheless it may be criticized for the absence of objective measurement of disease severity such as $FEV_1$.[35,36] In this regard, it is interesting to note that recent investigators have used the MRC to stage COPD severity in telephone surveys in Canada[37] and in America.[33]

The aim of the present study was to assess whether the MRC dyspnoea scale might also be useful during telephone surveys as a fast and reliable way of rating perceived health status in elderly patients with COPD.

## Materials and methods

### Study population

After giving consent, a sample of 200 Italian home dwelling COPD patients over 64 years of age underwent a comprehensive health status assessment by telephone interview. Patients were randomly selected from an administrative database of patients having a spirometrically confirmed diagnosis of COPD and regularly followed by respiratory physicians. Thus, the studied sample is representative of elderly COPD patients receiving specialist care. The survey was conducted in April 2008. It conformed to guidelines provided by the Ethical Committee of the Campus Bio-Medico University.

### Survey questionnaire

The telephone survey contained 71 items and took approximately 40 min to complete. Survey questions were conceived and written by the investigators and GfK Eurisko Health Care Department. Interviewers experienced with telephone and population-based surveys conducted the telephone interviews from a script to ensure consistency amongst all interviewers. Because this was the first time the questionnaire had been used, it was piloted to ensure that questions and responses were unambiguous to respondents.

The telephone-based interview was performed to evaluate the degree of disability imposed by COPD on the population surveyed. Interviewers first ascertained whether respondents met study inclusion criteria of having a physician and spirometrically confirmed diagnosis of COPD, were 64 years of age or older and had a smoking history. Educational level, financial status, living arrangements and social contacts were also ascertained. The remainder of the interview used the questionnaire to explore the impact that COPD had on the lives of the respondents. Information requested included: duration of COPD, symptoms, pharmacotherapy used, use of supplemental oxygen, experience with pulmonary rehabilitation, frequency of emergency room visits and hospitalizations and the presence of co-morbid illness. Interviewers also probed the impact that COPD had on patient-centred values including: perceived health and emotional status, limitations in social life and in activities of daily living (ADL), and pain-related limitations in activities of daily living. To evaluate the perceived health status we used a simple Likert scale with values from 1 (low quality) to 5 (excellent). Similarly, emotional status was quantified by asking how long the patient had felt sad during the past 4 weeks (scale from 1 = never, to 6 = always). Limitations in social life were measured by a scale from 1 (never) to 5 (always), whereas limitations in activities of daily living were quantified using a scale from 0 (no limitation) to 2 (1 = partially limited, 2 = totally limited). For pain-related limitations we used a similar scale ranging from

0 (no limitations) to 4 (totally limited). Assessment of functional status was done using both the basic ADL and instrumental ADL (IADL) scales. Basic ADL are activities allowing people to live at home with some external help and consist of items such as having a bath, dressing, going to toilette, issues with bowel continence, moving from bed to chair, eating, etc. IADL are activities associated with being independent indoors, such as use of telephone, cooking, taking care of the home, washing clothes, taking medications, etc. and with outdoor independence, including doing the shopping, going out, managing money, etc. According to this hierarchy, IADL are usually lost before ADL, but occasionally selected ADL, e.g. urinary continence, may be lost despite well preserved IADL.

MRC dyspnoea scale and IADL scale were widely used for postal and telephone surveys in previous studies, furthermore ADL scale was formally validated in these contexts.[38–43] Subjects were classified according to symptom severity using the MRC dyspnoea scale based on their responses to questions about breathlessness posed by the interviewers (Table 1). In order to simplify analysis, we defined an MRC scale of 1 as ''mild'' dyspnoea, an MRC scale of 2–3 as ''moderate'' dyspnoea and an MRC scale of 4–5 as ''severe'' dyspnoea.

### Statistical analysis

Statistical analysis of all variables was conducted using commercially available software (Statistica '99 Edition for Windows). Frequencies or percentages were used to describe nominal data.

Based on reported MRC scores, we categorized patients into 3 groups: mild, moderate and severe and then compared these MRC-based groups with various survey response items. A chi-square test was employed when testing for differences between the 3 groups of patients for nominal data. To assess differences amongst group mean values, we used analysis of variance (ANOVA) for variables with a normal distribution, or the Kruskal–Wallis test for those variables that were not normally distributed. Post hoc comparison between groups for continuous variables was made by the Tukey test.[44] Statistical significance for all analysis was accepted at a level of $p < 0.05$.

**Table 1** MRC Scale and Severity Categories.

| MRC Grade | Description | MRC Severity Grouping |
|---|---|---|
| 1 | Breathless with strenuous exercise | MILD |
| 2 | Short of breath when hurrying on the level or walking up a slight hill | MODERATE |
| 3 | Walks slower than people of the same age on the level or stops for breath while walking at own pace on the level | |
| 4 | Stops for breath after walking 100 m | SEVERE |
| 5 | Too breathless to leave the house or breathless when dressing | |

## Results

### Demographics

Patient demographics are listed in Table 2. Two hundred patients (146 male, 54 female) with a mean age of $74.4 \pm 6.2$ years were enrolled in the survey. Ages ranged from 65 years to over age 80 and were fairly evenly distributed: 23% aged 65-69 years, 32% aged 70–74 years, 21% aged 75–79 years and 24% aged 80 years or above. Patients were also evenly distributed geographically with 23% living in the north-west of Italy, 15% in the north-east, 20% in central Italy and 42% in the south and/or the islands. The majority of patients had at least an elementary school level of education (80%) and consistent with the advanced age of respondents, 89% were retired.

### Severity and impact of COPD on symptoms and health status

Classification of patients by MRC score and the mean MRC scores are shown in Table 3. The majority of patients (62%) interviewed reported moderate or severe dyspnoea as defined by MRC groupings. Table 4 shows the average values for various patient demographics based on MRC severity groupings. Patients in the three MRC severity groups did not differ significantly by age, geographic location or smoking burden as assessed by pack years. Patients with the most severe COPD by MRC score had less formal education than patients with mild disease.

Table 5 shows the relationship between MRC dyspnoea groupings and various disease impact parameters. Most of the recorded indicators of health status worsened progressively with MRC severity score. Although there was no statistically significant correlation of basic ADL scores and dyspnoea grade, there were significant differences in IADL amongst all MRC severity scores. Statistically significant differences were also found among the 3 MRC severity scores for perceived health status, emotional status, pain-

**Table 2** Patient demographics.

| | Population (200 patients) | |
|---|---|---|
| Age (years) | 65–69 | 23% |
| | 70–74 | 32% |
| | 75–79 | 21% |
| | >80 | 24% |
| Geographic location in Italy | North-West | 23% |
| | North-East | 15% |
| | Centre | 20% |
| | South & Islands | 42% |
| School education | No qualification | 22% |
| | Elementary school | 46% |
| | Lower middle school | 18% |
| | Higher middle school | 12% |
| | University | 2% |
| Employment status | Currently working | 1% |
| | Retired | 89% |
| | Unemployed | 1% |
| | Housewife | 9% |

**Table 3** Distribution of MRC severity scores in population sampled.

| MRC Dyspnoea Classification | Number of patients (% total) | Mean MRC Score |
|---|---|---|
| ''Mild'' (MRC 1) | 76 (38%) | 1 |
| ''Moderate'' (MRC 2–3) | 53 (26.5%) | 2.3 |
| ''Severe'' (MRC 4–5) | 71 (35.5%) | 4.5 |

related limitations and limitations in social life. Patients with MRC ''severe'' scores had significantly more hospital admissions in the preceding year than those with MRC ''mild'' and ''moderate'' scores (1.56, 1.07 and 0.43 per year respectively) and patients with MRC ''moderate'' scores had more hospitalizations than those with MRC ''mild'' scores. Patients with MRC ''severe'' scores also had more emergency department visits in the preceding year than patients with MRC scores of ''moderate'' and ''mild'' severity, but no differences were seen in the number of emergency department visits between patients with MRC ''mild'' versus ''moderate'' severity scores.

The prevalence of comorbidity was also tracked by MRC severity score. Fig. 1 demonstrates that co-morbid illnesses were significantly more prevalent in patients with MRC ''severe'' scores compared to those with MRC ''mild'' severity (4.94 versus 2.67). Fig. 2 illustrates prevalence of individual co-morbidities according to MRC severity score. There were significant differences amongst patients with MRC ''mild', ''moderate'' and ''severe'' scores with regard to the prevalence of heart disease, diabetes, hypertension, osteoporosis and fractures. The need for long-term oxygen therapy was also tracked by MRC severity score (10.5%, 41.5%, 59.6% respectively). There were no significant differences by MRC severity score for use of pulmonary rehabilitation, duration of COPD, or living arrangements and social contacts.

## Discussion

This study confirms that in an elderly COPD population, telephone administration of the MRC dyspnoea severity score can be used as a simple, robust surrogate marker of health status, summarizing several important variables pertaining to mood, personal independence and use of health care resources. Thus, rating dyspnoea with the MRC scale convincingly classifies elderly COPD patients according to their health status and the burden imposed by the disease. This makes MRC a very useful tool for epidemiological purposes. However, the lack of information on its responsiveness when administered through telephone prevents us form recommending it for the follow up of the individual patient.

Compared to basic ADLs, the relationship between MRC and personal independence was more evident for IADLs, which showed a progressive decline with increasing MRC scores. This is not surprising, given that IADLs cover a broad range of individual capabilities which are lost earlier and more gradually than ADLs.[45] Patients experience limitations in ADLs when their clinical status is dramatically worsened, which corresponds to an MRC severity threshold of 4. An MRC severity score $\geq 4$ thus targets truly disabled individuals highly dependent on external help for activities of daily living. This finding reflects the true heterogeneity of health status in COPD population, confirming previous findings by several investigators.[20,21,46–51]

The MRC score may be a good surrogate for formal health status assessment because it is likely not just a marker of lung dysfunction. It is likely that co-morbidity, whose burden paralleled MRC severity, contributes to the MRC severity score and thus to health status. For example, left heart dysfunction could worsen dyspnoea. Similarly, thoracic vertebral compression fractures associated with osteoporosis may worsen dyspnoea by induction of a restrictive ventilatory deficit, as fracture of a thoracic vertebral body can decrease the vital capacity by 4–7%.[52] Furthermore, osteoporosis might be responsible for pain-related limitations, which in our patients amounted to a significant 81% prevalence (15.5% mild, 31.5% moderate, 26.5% severe, 7.5% very severe limitations). Pain is not among the symptoms usually asked about in COPD patients, but our data show that it is highly prevalent and disabling.

We also observed that the MRC severity score was a marker of health care resource needs as expressed by

**Table 4** Relationship of MRC severity classification to patient demographics.

| | Mean (SD) | | |
|---|---|---|---|
| | MRC ''Mild'' (76) | MRC ''Moderate'' (53) | MRC ''Severe'' (71) |
| Age (years) | 72.7 | 74.3 | 76.4 |
| Smoking burden (pack years) | 30.1 (27) | 36.4 (30) | 31.5 (29) |
| School Education (years) | 7.0[a] (3.54) | 6.28 (4.33) | 5.4[a] (3.01) |
| Number of people living with patient | 1.3 (1.08) | 1.3 (0.76) | 1.3 (0.89) |
| Sex | 75% Male; 25% Female | 73.6% Male; 26.4% Female | 70.4% Male; 29.6% Female |
| Geographic location | | | |
| North-West | 30.30% | 17% | 21.10% |
| North-East | 15.80% | 17% | 12.70% |
| Centre | 23.70% | 22.60% | 12.70% |
| South & Islands | 30.20% | 43.40% | 53.50% |

[a] $p = 0.02$ MRC ''Severe'' vs. MRC ''Mild''.

**Table 5** Relationship of MRC severity classification to COPD impact.

| | MRC ''Mild'' (76) | MRC ''Moderate'' (53) | MRC ''Severe'' (71) | Test HSD Tukey (*p* value) | | |
|---|---|---|---|---|---|---|
| | Mean (SD) | Mean (SD) | Mean (SD) | ''Mild'' vs ''Moderate'' | ''Mild'' vs ''Severe'' | ''Moderate'' vs ''Severe'' |
| ADL score | 5.66 (0,81) | 5.23 (0,95) | 3.53 (1,79) | n.s.[b] | <0.001 | <0.001 |
| IADL score | 7.49 (1,26) | 5.83 (2,34) | 3.46 (2,12) | <0.001 | <0.001 | <0.001 |
| Perceived health status | 2.71 (0,69) | 1.98 (0,8) | 1.48 (0,67) | <0.001 | <0.001 | <0.001 |
| Emotional status | 2.22 (0,68) | 2.62 (0,76) | 3.03 (1) | 0.0197 | <0.001 | 0.0194 |
| Pain-related limitation | 1.00 (1,02) | 2.04 (1,04) | 2.76 (0,8) | <0.001 | <0.001 | <0.001 |
| Limitation in social life | 1.97 (0,83) | 2.94 (0,89) | 3.39 (0,82) | <0.001 | <0.001 | 0.0089 |
| Limitation moderate physical activity | 0.67 (0,66) | 1.26 (0,59) | 1.73 (0,5) | <0.001 | <0.001 | <0.001 |
| Limitation stairs | 0.67 (0,66) | 1.30 (0,61) | 1.72 (0,51) | <0.001 | <0.001 | <0.001 |
| Hospital admissions last year | 0.43 (0,66) | 1.07 (1,28) | 1.56 (1,36) | 0.004 | <0.001 | 0.0437 |
| ED visits last year | 0.18 (0,58) | 0.55 (1.05) | 1.21 (1,44) | n.s.[b] | <0.001 | 0.0019 |
| Number of co-morbid illnesses | 2.67 (1,69) | 3.38 (2) | 4.94 (2,15) | n.s.[b] | <0.001 | <0.001 |
| % patients on long-term oxygen | 10.50% | 41.50% | 59.20% | <0.001[a] | <0.00[a] | <0.001[a] |

[a] chi-square test.
[b] statistically non-significant.

hospital and emergency department admissions in the preceding year and by the use of supplementary oxygen. This observation deserves consideration because although respiratory symptoms are important, non-respiratory problems are known to be main determinants of the need to access health care resources. Non-respiratory causes trigger up to 60% of admission of COPD patients,[53–57] and the cost of hospital care is directly related to the number of co-morbid conditions.[58–61] Thus, dyspnoea as quantified by the MRC score can function as a marker of the need to access health care resources, perhaps because as we have shown, it is a robust indicator of overall health status in COPD. It is of interest that the fraction of patients undergoing rehabilitation did not increase for increasing MRC score (11.8% patients with mild dyspnoea, 22.6% with moderate and 15.5% with severe dyspnoea) This may reflect the availability or lack of availability of pulmonary rehabilitation in the population surveyed, as well as physician prescribing practices. Whichever is the explanation, it is disturbing that about half patients regularly cared by respiratory physicians never underwent a non pharmacological intervention of proved efficacy even in very severe COPD.[62–67]

The availability of an easy to use telephone-based assessment instrument that reflects health status is of special interest for both clinical and epidemiological purposes. The MRC scale can be used for quick assessment or for large surveys. In the latter instance, its measurement properties could permit stratification of patients according to COPD-related health status impairment. It also is likely, yet unproved, that MRC scale qualifies as a telephone marker of individual response to therapeutic interventions, similar to the way it has been used in traditional ambulatory-based studies.[21–25,62] More important, telephone-based assessments of disability are of special interest in patient

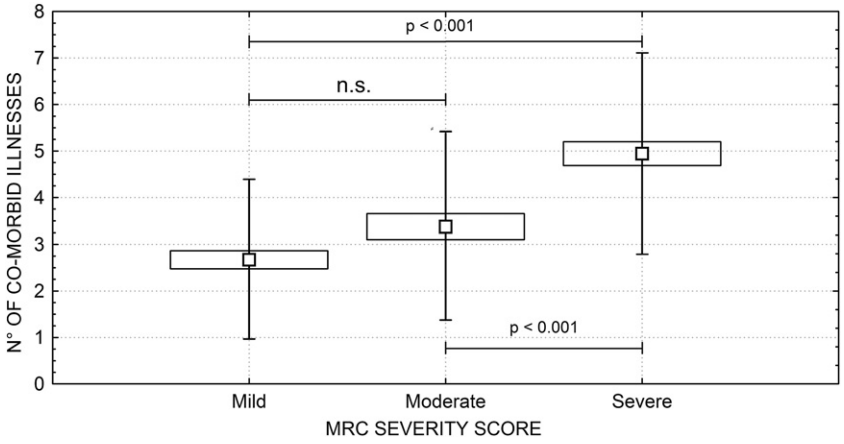


**Figure 1** Number of co-morbid illnesses related to MRC severity score.

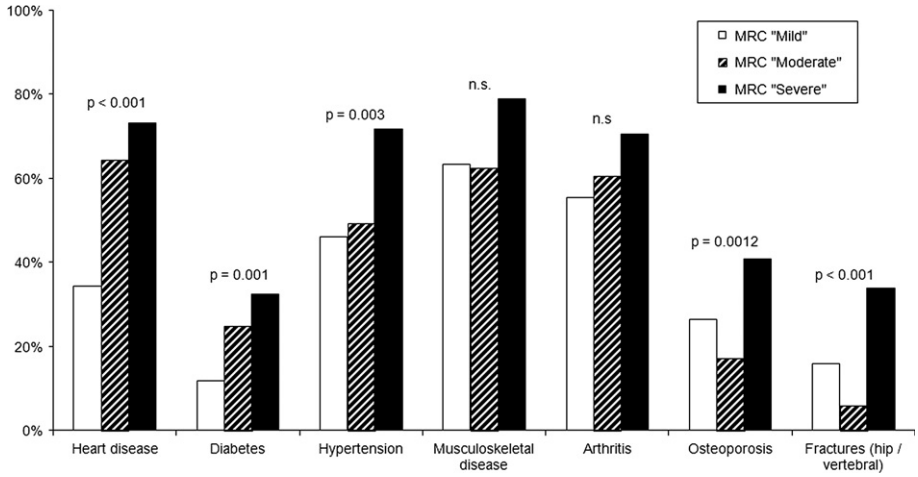


**Figure 2** Prevalence of specific co-morbidities by MRC dyspnoea group.

populations experiencing severe limitations in mobility. In our series 16% of the total population enrolled were not able to leave their homes due to breathlessness or other limitations, and in other studies on elderly COPD populations, the prevalence of home confined subjects ranged between 11.9% and 34%.[21,35] Thus, a consistent proportion of patients would be and actually is excluded from both clinical trials and epidemiological studies because they are confined at home, The MRC-based telephone surveys allows to take into consideration these people at least for epidemiological purposes or clinical screening studies.

Limitations of this study deserve consideration. First, patients were representative of a COPD population under regular specialist care and not of the general COPD population. Furthermore, we had no access to lung function data and thus, were not able to correlate our findings with $FEV_1$-based disease severity assessment. Second, females were underrepresented (73% male, 27% female), which makes our results more tailored to an elderly male COPD population. Thirdly, some components of this questionnaire had not been previously validated for telephone survey.

Notwithstanding these limitations, the results from our survey are similar to those obtained from two recent telephone surveys of COPD patients in Canada[37] and America[33]with regard to the relationship between MRC score and health status impairment Both of these surveys also relied upon physician diagnosis of COPD and did not have access to $FEV_1$ data. The Canadian and American surveys did not restrict the age of respondents to the elderly as we did in our survey (mean age 74.4 years), but both assessed COPD severity using the MRC dyspnoea scale. Furthermore, using the MRC dyspnoea groupings used in our study, the distributions of ''mild'', ''moderate'' and ''severe'' dyspnoea grades were 26%, 44%, 26% in the Canadian survey[37] and 12%, 50%, 36% in the American study[33] vs. 38%, 26.5% and 35.5% in our sample. Thus, the important analogies in the MRC-health status relationship among different COPD populations supports the interpretation of COPD as a condition with a distinctive impact on health status and that of MRC as a reliable surrogate health status index.

In conclusion, this study shows that the MRC dyspnoea severity score can also function as a simple surrogate for health status and multidimensional assessment. On the basis of our data, an MRC score $> 3$ would mark a severely impaired health status. It is highly suitable for telephone surveys of COPD patients for epidemiological purposes. However, our study explored only the classification properties of the MRC score in an elderly population. Further research is needed to assess both responsiveness and predictivity of the telephone-recorded MRC score with regard to other patient-centred outcomes in COPD patients of all ages. Clarifying these properties will allow verify to which extent MRC can be effectively administered through telephone for clinical purposes.

## Conflict of interest statement

None.

## References

1. Buist AS, Vollmer WM, Sullivan SD, et al. The burden of obstructive lung disease initiative (BOLD): rationale and design. *COPD* 2005;**2**(2):277—83.
2. Global initiative for chronic obstructive lung disease. Guidelines: workshop report; global strategy for diagnosis, management, and prevention of COPD, updated; November 2008.
3. Celli BR, MacNee W, Agusti A, et al. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J* 2004;**23**:932—46.
4. Killian KJ, Leblanc P, Martin DH, Summers E, Jones NL, Campbell EJ. Exercise capacity and ventilatory, circulatory and symptom limitation in patients with chronic airflow obstruction. *Am Rev Respir Dis* 1992;**146**:935—40.
5. Ferrer M, Alonso J, Morera J, et al. Chronic obstructive pulmonary disease stage and health-related quality of life. *Ann Int Med* 1997;**127**:1072—9.
6. Curtis J, Deyo R, Hudson L. Health-related quality of life among patients with chronic obstructive pulmonary disease. *Thorax* 1994;**49**:162—70.
7. Partridge M. Living with COPD: the patients' perspective. *Eur Respir Rev*; 2004:1—5.
8. Jenkins C, Rodriquez-Roisin R. Quality of life, stage severity and COPD. *Eur Respir J* 2009;**33**:953—5.
9. Jones PW. Health status measurement in chronic obstructive pulmonary disease. *Thorax* 2001;**56**:880—7.

10. Guyatt GH, King DR, Feeny DH, Stubbing D, Goldstein RS. Generic and specific measurement of health-related quality of life in a clinical trial of respiratory rehabilitation. *J Clin Epidemiol* 1999;**52**:187–92.
11. Jones PW, Quirk FH, Baveystock CM, Littlejohns P. A self-complete measure of health status for chronic airflow limitation: the St George respiratory questionnaire. *Am Rev Respir Dis* 1992;**145**:1321–7.
12. Guyatt GH, Berman LB, Townsend M, Pugsley SO, Chambers LW. A measure of quality of life for clinical trials in chronic lung disease. *Thorax* 1987;**42**:773–8.
13. Tsai C, Hodder R, Page J, et al. The short-form chronic respiratory disease questionnaire was a valid, reliable, and responsive quality-of-life instrument in acute exacerbations of chronic obstructive pulmonary disease. *J Clin Epidemiol* 2008; **61**:489–97.
14. Fletcher CM, Elmes PC, Wood CH. The significance of respiratory symptoms and the diagnosis of chronic bronchitis in a working population. *BMJ* 1959;**2**:257–66.
15. Mahler DA, Weinberg DH, Wells CK, Feinstein AR. The measurement of dyspnea: contents, interobserver agreement, and physiologic correlates of two new clinical indexes. *Chest* 1984;**85**:751–8.
16. Hajiro T, Nishimura K, Tsukino M, Ikeda A, Koyama H, Izumi T. Comparison of discriminative properties among disease specific questionnaires for measuring health-related quality of life in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1998;**157**:785–90.
17. Oga T, Nishimura K, Tsukino M, et al. Longitudinal deteriorations in patient reported outcomes in patients with COPD. *Resp Med* 2007;**101**(1):146–53.
18. Miravitlles M, Llor C, de Castellar R, et al. Validation of the COPD severity score for use in primary care: the NEREA study. *Eur Respir J* 2009;**33**:519.
19. Evans RA, Singh SJ, Collier R, Williams JE, Morgan MD. Pulmonary rehabilitation is successful for COPD irrespective of MRC dyspnoea grade. *Respir Med* 2009;**103**(7):1070–5.
20. Celli BR, Cote CG, Marin JM, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med* 2004;**350**: 1005–12.
21. Nishimura K, Izumi T, Tsukino M, Oga T. Dyspnea is a better predictor of 5-year survival than airway obstruction in patients with COPD. *Chest* 2002;**121**:1434–40.
22. Hernández MT, Rubio TM, Ruiz FO, Riera HS, Gil RS, Gómez JC. Results of a home-based training program for patients with COPD. *Chest* 2000;**118**:106–14.
23. Akamatsu K, Yamagata T, Takahashi T, et al. Improvement of pulmonary function and dyspnea by tiotropium in COPD patients using a transdermal beta(2)-agonist. *Pulm Pharmacol Ther* 2007;**20**(6):701–7.
24. De Torres JP, Pinto-Plata V, Ingenito E, et al. Power of outcome measurements to detect clinically significant changes in pulmonary rehabilitation of patients with COPD. *Chest* 2002; **121**:1092–8.
25. Kardos P, Wencker M, Glaab T, Vogelmeier C. Impact of salmeterol/fluticasone propionate versus salmeterol on exacerbations in severe chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2007;**175**:144–9.
26. Bestall JC, Paul EA, Garrod R, Garnham R, Jones PW, Wedzicha JA. Usefulness of the medical research council dyspnoea scale as a measure of disability in patients with COPD. *Thorax* 1999;**54**:581–6.
27. O'Donnell DE, Aaron S, Bourbeau J, et al. Canadian thoracic society recommendations for management of chronic obstructive pulmonary disease–2007 update. *Can Respir J* 2007;**14**:5B.
28. Riegel B, Carlson B, Kopp Z, LePetri B, Glaser D, Unger A. Effect of a standardized nurse case-management telephone intervention on resource use in patients with chronic heart failure. *Arch Intern Med* 2002;**162**:705–12.
29. Austin JS, Maisiak RS, Macrina DM, Heck LW. Health outcome improvements in patients with systemic lupus erythematosus using two telephone counseling interventions. *Arthritis Care Res* 1996;**9**:391–9.
30. Mohr DC, Likosky W, Bertagnolli A, et al. Telephone-administered cognitive-behavioral therapy for the treatment of depressive symptoms in multiple sclerosis. *J Consult Clin Psychol* 2000;**68**:356–61.
31. Simon GE, VonKorff M, Rutter C, Wagner E. Randomised trial of monitoring, feedback, and management of care by telephone to improve treatment of depression in primary care. *BMJ* 2000; **320**:550–4.
32. Piette JD, Weinberger M, McPhee SJ. The effect of automated calls with telephone nurse follow-up on patient-centered outcomes of diabetes care: a randomized, controlled trial. *Med Care* 2000;**38**:218–30.
33. Barr RG, Celli BR, Mannino DM, et al. Comorbidities, patient knowledge and disease management in a national sample of patients with COPD. *Am J Med* 2009;**122**(4):348–55.
34. Eisner M, Trupin L, Katz P, et al. Development and validation of a survey-based COPD severity score. *Chest* 2005;**127**(6): 1890–7.
35. Miravitlles M, de la Roza C, Morera J, et al. Chronic respiratory symptoms, spirometry and knowledge of COPD among general population. *Respir Med* 2006;**100**(11):1973–80.
36. Mularski RA, Asch SM, Shrank WH, et al. The quality of obstructive lung disease care for adults in the United States as measured by adherence to recommended processes. *Chest* 2006;**130**(6):1844–50.
37. Hernandez P, Balter M, Bourbeau J, Hodder R. Living with chronic obstructive pulmonary disease: a survey of patients' knowledge and attitudes. *Respir Med* 2009;**103**(7): 1004–12.
38. Huijnen B, Van Der Horst F, van Amelsvoort L, et al. Dyspnoea in elderly family practice patients. Occurrence, severity, quality of life and mortality over an 8-year period. *Fam Pract* 2006;**23**(1):34–9.
39. Ho SF, O'Mahony MS, Steward JA, Breay P, Buchalter M, Burr ML. Dyspnoea and quality of life in older people at home. *Age and Ageing* 2001;**30**(2):155–9.
40. Rennard S, Decramer M, Calverley PMA, et al. Impact of COPD in North America and Europe in 2000: Subjects' perspective of confronting COPD International survey. *Eur Respir J* 2002;**20**: 799–805.
41. Appleton S, Adams R, Porter S, Peacock M, Ruffin R. Sustained improvements in dyspnoea and pulmonary function 3 to 5 years after lung volume reduction surgery. *Chest* 2003; **123**:1838–46.
42. Shinar D, Gross CR, Bronstein KS, et al. Reliability of the activities of daily living scale and its use in telephone interview. *Arch Phys Med Rehabil* 1987;**68**(10):723–8.
43. Ciesla JR, Shi L, Stoskopf CH, Samuels ME. Reliability of kat's activities of daily living scale when used in telephone interview. *Eval Health Prof* 1993;**16**(2):190–203.
44. Altman DG. *Practical statistics for medical research*. Chapman and Hall; 1991.
45. Nikolova R, Demers R, Beland F. Trajectories of cognitive decline in functional status in the frail older adults. *Arch Gerontol Geriatr* 2009;**48**(1):28–34.
46. Antonelli Incalzi R, Fuso L, De Rosa M, et al. Co-morbidity contributes to predict mortality of patients with chronic obstructive pulmonary disease. *Eur Respir J* 1997;**10**: 2794–800.
47. Kanner RE, Renzetti AD, Stanish WM, Barkman HW, Klauber MR. Predictors of survival in subjects with chronic airflow limitation. *Am J Med* 1983;**74**:249–55.

48. Anthonisen NR. Prognosis in chronic obstructive pulmonary disease: results from multicenter clinical trials. *Am Rev Respir Dis* 1989;**140**:S95—S99.
49. Burrows B, Bloom JW, Traver GA, Cline MG. The course and prognosis of different forms of chronic airways obstruction in a sample from the general population. *N Engl J Med* 1987;**317**: 1309—14.
50. Schellevis FG, Van der Velden J, Van de Lisdonk E, Van Eijk JM, Van Weel C. Co-morbidity of chronic diseases in general practice. *J Clin Epidemiol* 1993;**46**:469—73.
51. Antonelli Incalzi R, Imperiale C, Bellia V, et al. Do GOLD stages of COPD severity really correspond to difference in health status? *Eur Respir J* 2003;**22**(3):444—9.
52. Biskobing DM. COPD and osteoporosis. *Chest* 2002;**121**:609—20.
53. Holguin F, Folch E, Redd SC, Mannino DM. Comorbidity and mortality in COPD-related hospitalizations in the United States, 1979 to 2001. *Chest* 2005;**128**:2005—11.
54. Mannino DM. COPD: Epidemiology, prevalence, morbidity and mortality, and disease heterogeneity. *Chest* 2002;**121**: 121S—126S.
55. Anthonisen NR, Connett JE, Enright PL, Manfreda J. Lung health study research group. hospitalizations and mortality in the lung health study. *Am J Respir Crit Care Med* 2002;**166**: 333—9.
56. Sidney S, Sorel M, Quesenberry Jr CP, DeLuise C, Lanes S, Eisner MD. COPD and incident cardiovascular disease hospitalizations and mortality: kaiser permanente medical care program. *Chest* 2005;**128**:2068—75.
57. Curkendall SM, DeLuise C, Jones JK, et al. Cardiovascular disease in patients with chronic obstructive pulmonary disease, Saskatchewan Canada cardiovascular disease in COPD patients. *Ann Epidemiol* 2006;**16**:63—70.
58. Kinnunen T, Saynajakangas O, Tuuponen T, Keistinen T. Impact of comorbidities on the duration of COPD patients' hospital episodes. *Respir Med* 2003;**97**:143—6.
59. Ward MM, Javitz HS, Smith WM, Bakst A, Orzolek WS. Cost of hospitalizations for COPD: a comparison of three approaches for attributing cost diagnosis. *Abstr Book Assoc Health Serv Res Meet* 1998;**15**:304—5.
60. Dal Negro R, Rossi A, Cerveri I. The burden of COPD in Italy: results from the confronting COPd survey. *Respir Med* 2003;**97**: 43—50. Suppl C.
61. Wouters EF. Economic analysis of the confronting COPD survey: an overview of results. Suppl C. *Respir Med* 2003;**97**:S3—S14.
62. Sweer L, Zwillich CW. Dyspnea in the patient with chronic obstructive pulmonary disease: etiology and management. *Clin Chest Med* 1990;**11**:417—45.
63. Goldstein RS, Gort EH, Stubbing D, Avendano MA. GuyattvGH. Randomised controlled trial of respiratory rehabilitation. *Lancet* 1994;**344**:1394—7.
64. Niederman MS, Clemente PH, Fein AM, et al. Benefits of a multidisciplinary pulmonary rehabilitation program. *Chest* 1991;**99**(4):798—804.
65. Zu Wallack RL, Patel K, Reardon JZ, Clark BA, Normandin EA. Predictors of improvement in the 12-minute walking distance following a six-week outpatients pulmonary rehabilitation program. *Chest* 1991;**99**:805—8.
66. Maltais F, Le Blanc P, Jobin J, et al. Intensity of training and physiologic adaptation in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1997;**155**(2): 555—61.
67. Restrick LJ, Paul EA, Braid GM, Cullinan P, Moore-Gillon J, Wedzicha JA. Assessment and follow up of patients prescribed long term oxygen therapy. *Thorax* 1993;**48**:708—13.